

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:

- (A) NAME: CIBA-GEIGY AG
- (B) STREET: Klybeckstr. 141
- (C) CITY: Basel
- (E) COUNTRY: Switzerland
- (F) POSTAL CODE (ZIP): 4002
- (G) TELEPHONE: +41 61 69 11 11
- (H) TELEFAX: + 41 61 696 79 76
- (I) TELEX: 962 991

(ii) TITLE OF INVENTION: New process for the production of  
biologically active protein

(iii) NUMBER OF SEQUENCES: 12

(iv) COMPUTER READABLE FORM:

- (A) MEDIUM TYPE: Floppy disk
- (B) COMPUTER: IBM PC compatible
- (C) OPERATING SYSTEM: PC-DOS/MS-DOS
- (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 339 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(vii) IMMEDIATE SOURCE:

(B) CLONE: E. coli LC137/pPLMu.hTGF-beta1 (DSM 5656)

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION:1..336

(D) OTHER INFORMATION:/product= "human TGF-beta1"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

GCC CTG GAC ACC AAC TAT TGC TTC AGC TCC ACG GAG AAG AAC TGC TGC	48
Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys	
1 5 10 15	
GTG CGG CAG CTG TAC ATT GAC TTC CGC AAG GAC CTC GGC TGG AAG TGG	96
Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp	
20 25 30	
ATC CAC GAG CCC AAG GGC TAC CAT GCC AAC TTC TGC CTC GGG CCC TGC	144
Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys	
35 40 45	
CCC TAC ATT TGG AGC CTG GAC ACG CAG TAC AGC AAG GTC CTG GCC CTG	192
Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu	
50 55 60	
TAC AAC CAG CAT AAC CCG GGC GCC TCG GCG GCG CCG TGC TGC GTG CCG	240
Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro	
65 70 75 80	
CAG GCG CTG GAG CCG CTG CCC ATC GTG TAC TAC GTG GGC CGC AAG CCC	288

Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro  
85 90 95

AAG GTG GAG CAG CTG TCC AAC ATG ATC GTG CGC TCC TGC AAG TGC AGC 336  
Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser  
100 105 110

TGA 339

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys  
1 5 10 15

Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp  
20 25 30

Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys  
35 40 45

Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu  
50 55 60

Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro  
65 70 75 80

Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro  
85 90 95

Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser  
100 105 110

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 339 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(vii) IMMEDIATE SOURCE:

- (B) CLONE: E. coli LC137/pPIMu.hTGF-beta2 (DSM5657)

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION:1..336
- (D) OTHER INFORMATION:/product= "human TGF-beta2"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

GCT TTG GAT GCG GCC TAT TGC TTT AGA AAT GTG CAG GAT AAT TGC TGC	48
Ala Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys	
115 120 125	
CTA CGT CCA CTT TAC ATT GAT TTC AAG AGG GAT CTA GGG TGG AAA TGG	96
Leu Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp	
130 135 140	
ATA CAC GAA CCC AAA GGG TAC AAT GGC AAC TTC TGT GCT GGA GCA TGC	144
Ile His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys	

145	150	155	160	
CCG TAT TTA TGG AGT TCA GAC ACT CAG CAC AGC AGG GTC CTG AGC TTA	192			
Pro Tyr Leu Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu				
165	170	175		
TAT AAT ACC ATA AAT CCA GAA GCA TCT GCT TCT CCT TGC TGC GTG TCC	240			
Tyr Asn Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser				
180	185	190		
CAA GAT TTA GAA CCT CTA ACC ATT CTC TAC TAC ATT GGC AAA ACA CCC	288			
Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro				
195	200	205		
AAG ATT GAA CAG CTT TCT AAT ATG ATT GTA AAG TCT TGC AAA TGC AGC	336			
Lys Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser				
210	215	220		
TAA				339

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 112 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Ala Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys			
1	5	10	15
Leu Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp			
20	25	30	

Ile His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys  
35 40 45

Pro Tyr Leu Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu  
50 55 60

Tyr Asn Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser  
65 70 75 80

Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro  
85 90 95

Lys Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser  
100 105 110

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 339 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(vii) IMMEDIATE SOURCE:

- (B) CLONE: E. coli LC137/pPIMu.hTGF-beta3 (DSM 5658)

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..336
- (D) OTHER INFORMATION: /product= "human TGF-beta3"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

GCT TTG GAC ACC AAT TAC TGC TTC CGC AAC TTG GAG GAG AAC TGC TGT	48
Ala Leu Asp Thr Asn Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys	
115 120 125	
GTG CGC CCC CTC TAC ATT GAC TTC CGA CAG GAT CTG GGC TGG AAG TGG	96
Val Arg Pro Leu Tyr Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp	
130 135 140	
GTC CAT GAA CCT AAG GGC TAC TAT GGC AAC TTC TGC TCA GGC OCT TGC	144
Val His Glu Pro Lys Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys	
145 150 155 160	
CCA TAC CTC CGC AGT GCA GAC ACA ACC CAC AGC ACG GTG CTG GGA CTG	192
Pro Tyr Leu Arg Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu	
165 170 175	
TAC AAC ACT CTG AAC CCT GAA GCA TCT GCC TCG CCT TGC TGC GTG CCC	240
Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro	
180 185 190	
CAG GAC CTG GAG CCC CTG ACC ATC CTG TAC TAT GTT GGG AGG ACC CCC	288
Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro	
195 200 205	
AAA GTG GAG CAG CTC TCC AAC ATG GTG GTG AAG TCT TGT AAA TGT AGC	336
Lys Val Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser	
210 215 220	
TGA	339

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 112 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

Ala Leu Asp Thr Asn Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys  
1 5 10 15

Val Arg Pro Leu Tyr Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp  
20 25 30

Val His Glu Pro Lys Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys  
35 40 45

Pro Tyr Leu Arg Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu  
50 55 60

Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro  
65 70 75 80

Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro  
85 90 95

Lys Val Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
100 105 110

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 336 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "recombinant hybrid DNA of



TGF-beta1 and TGF-beta3 DNA"

(vii) IMMEDIATE SOURCE:

(B) CLONE: E. coli LCL37/pPIMu.TGF-beta1(44/45)beta3

(ix) FEATURE:

(A) NAME/KEY: mat\_peptide

(B) LOCATION:1..132

(D) OTHER INFORMATION:/product= "N-terminal 44 amino acids of human TGF-beta1"

(ix) FEATURE:

(A) NAME/KEY: mat\_peptide

(B) LOCATION:133..336

(D) OTHER INFORMATION:/product= "C-terminal 68 amino acids of human TGF-beta3"

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION:1..336

(D) OTHER INFORMATION:/product= "hybrid TGF-beta named TGF-beta1-3"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

GCC CTG GAC ACC AAC TAT TGC TTC AGC TCC ACG GAG AAG AAC TGC TGC	48
Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys	
1 5 10 15	
GTG CGG CAG CTG TAC ATT GAC TTC CGC AAG GAC CTC GGC TGG AAG TGG	96
Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp	
20 25 30	
ATC CAC GAG CCC AAG GGC TAC CAT GCC AAC TTC TGC TCA GGC CCT TGC	144
Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Ser Gly Pro Cys	

45

TAC AAC ACT CTG AAC CCT GAA GCA TCT GGC TCG CCT TGC TGC GTG CCC 240  
Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro  
65 70 75 80

CAG GAC CTG GAG CCC CTG ACC ATC CTG TAC TAT GTT GGG AGG ACC CCC 288  
Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro  
85 90 95

AAA GTG GAG CAG CTC TOC AAC ATG GTG GTG AAG TCT TGT AAA TGT AGC 336  
Lys Val Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
100 105 110

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys  
1 5 10 15

Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp  
20 25 30

Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Ser Gly Pro Cys  
35 40 45

Pro Tyr Leu Arg Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu  
50 55 60

Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro  
65 70 75 80

Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro  
85 90 95

Lys Val Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
100 105 110

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 336 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(B) DESCRIPTION: /desc = "recombinant hybrid DNA  
coding for hybrid TGF-beta2-3"

(vii) IMMEDIATE SOURCE:

(B) CLONE: E. coli LC137/pPIMu.TGF-beta2(44/45)beta3

(ix) FEATURE:

- (A) NAME/KEY: mat\_peptide
- (B) LOCATION: 1..132
- (D) OTHER INFORMATION: /product= "N-terminal 44 amino  
acids of human TGF-beta2"

(ix) FEATURE:

(A) NAME/KEY: mat\_peptide  
(B) LOCATION:133..336  
(D) OTHER INFORMATION:/product= "C-terminal 68 amino acids of human TGF-beta3"

(ix) FEATURE:

(A) NAME/KEY: CDS  
(B) LOCATION:1..336  
(D) OTHER INFORMATION:/product= "hybrid TGF-beta2-3"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

GCT TTG GAT GCG GCC TAT TGC TTT AGA AAT GTG CAG GAT AAT TGC TGC	48
Ala Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys	
1 5 10 15	
CTA CGT CCA CTT TAC ATT GAT TTC AAG AGG GAT CTA GGG TGG AAA TGG	96
Leu Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp	
20 25 30	
ATA CAC GAA CCC AAA GGG TAC AAT GCC AAC TTC TGC TCA GGC CCT TGC	144
Ile His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ser Gly Pro Cys	
35 40 45	
CCA TAC CTC CGC AGT GCA GAC ACA ACC CAC AGC ACG GTG CTG GGA CTG	192
Pro Tyr Leu Arg Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu	
50 55 60	
TAC AAC ACT CTG AAC CCT GAA GCA TCT GCC TCG CCT TGC TGC GTG CCC	240
Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro	
65 70 75 80	
CAG GAC CTG GAG CCC CTG ACC ATC CTG TAC TAT GTT GGG AGG ACC CCC	288
Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro	
85 90 95	

AAA GTG GAG CAG CTC TCC AAC ATG GTG GTG AAG TCT TGT AAA TGT AGC 336  
Lys Val Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
100 105 110

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 112 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Ala Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys  
1 5 10 15  
Leu Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp  
20 25 30  
Ile His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ser Gly Pro Cys  
35 40 45  
Pro Tyr Leu Arg Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu  
50 55 60  
Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro  
65 70 75 80  
Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro  
85 90 95  
Lys Val Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
100 105 110

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 336 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "recombinant hybrid DNA  
coding for hybrid TGF-beta3-2"

(vii) IMMEDIATE SOURCE:

- (B) CLONE: E. coli LC137/pPLMu.TGF-beta3(44/45)beta2

(ix) FEATURE:

- (A) NAME/KEY: mat\_peptide
- (B) LOCATION:1..132
- (D) OTHER INFORMATION:/product= "N-terminal 44 amino  
acids of human TGF-beta3"

(ix) FEATURE:

- (A) NAME/KEY: mat\_peptide
- (B) LOCATION:133..336
- (D) OTHER INFORMATION:/product= "C-terminal 68 amino  
acids of human TGF-beta2"

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION:1..336
- (D) OTHER INFORMATION:/product= "hybrid TGF-beta3-2"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

GCT TTG GAC ACC AAT TAC TGC TTC CGC AAC TTG GAG GAG AAC TGC TGT

AAG ATT GAA CAG CTT TCT AAT ATG ATT GTA AAG TCT TGC AAA TGC AGC 336  
Lys Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser  
100 105 110

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12;

Ala Leu Asp Thr Asn Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys

1

5

10

15

Val Arg Pro Leu Tyr Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp

20

25

30

Val His Glu Pro Lys Gly Tyr Tyr Ala Asn Phe Cys Ala Gly Ala Cys

35

40

45

Pro Tyr Leu Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu

50

55

60

Tyr Asn Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser

65

70

75

80

Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro

85

90

95

Lys Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser

100

105

110